Are low-carbohydrate (

Conclusion

A moderate body of evidence demonstrates that diets with less than 45% of calories as carbohydrates are not more successful for long-term weight loss (12 months). There is also some evidence that they may be less safe. In shorter-term studies, low-calorie, high-protein diets may result in greater weight loss, but these differences are not sustained over time.

Grade: Moderate

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

This conclusion is based on 15 articles published since 2004: Three review articles, nine randomized controlled trials (RCTs) and four prospective cohort studies (Avenell, 2004; Dale, 2009; Due, 2008; Frisch, 2009; Halton, 2006; Halton, 2008; Hession, 2009; Lagiou, 2007; Lim, 2009; McAuley, 2005; Nordmann, 2006; Sacks, 2009; Shai, 2008; Tay, 2008; Trichopoulou, 2007). Studies were conducted in the Australia, Denmark, Germany, Greece, Israel, New Zealand, Sweden and the US. Studies ranged in length from six months to 24 months. Studies also ranged in sample size from 55 to 98,462 subjects and had drop-out rates from 12% to 34%. Diets tested ranged from 10% to 61% energy from fat, 15% to 36% energy fromprotein, and four to 70% energy from carbohydrate (CHO).

Nine studies found no difference in long-term (more than six months) weight loss between low-CHO (<45%) diets, compared to others differing in macronutrient proportion (Avenell, 2004; Dale, 2009; Due, 2008; Frisch, 2009; Lim, 2009; McAuley, 2005; Nordmann, 2006; Sacks, 2009; Tay, 2008). Two studies found that lower-CHO diets resulted in better long-term (more than six months) weight loss than low-fat, low-calorie diets (Hession, 2009; Tay, 2008).

One study found that high-CHO diets increased total and low-density lipoprotein cholesterol (LDL-C) compared to low-fat diets (Hession, 2009). One study found that a high-fat (monounsaturated fat) diet increased total cholesterol (TC) and LDL-C compared to a high-CHO diet (Dale, 2009). One study found that a high-fat diet increased LDL-C, compared to a high-protein diet (McAuley, 2005). Two studies found that diets lower in CHO and higher in protein were associated with increased total and cardiovascular mortality (Lagiou, 2007; Trichopoulou, 2007). One study found no association between low-CHO, high-protein diets and risk of cardiovascular disease(CVD) (Halton, 2006). One study found no associated between low-CHO, high-protein diets and risk of type 2 diabetes (T2D) (Halton, 2008).

Evidence summary paragraphs (15)

Systematic Reviews and Meta-Analyses (3)

Avenell et al, 2004 (positive quality) systematically reviewed RCTs published in the US and Europe to compare the effectiveness of various diets with at least one year of follow-up. The final sample included 26 RCTs which compared low-fat diets (LFD; advice given to reduce fat, more than 6.7MJ per day), low-calorie diets (LCD; 4.2-6.7MJ per day), or very-low-calorie diets (VLCD; less than 4.2MJ per day) with control treatment or compared to other types of diets, as well as protein-sparing modified fasts (PSMF; ≤40g per day of CHO) with LCDs and VLCDs. Low-fat diets produced significant weight losses up to 36 months (-3.55kg, 95% CI -4.54 to -2.55kg), and improved blood pressure (BP), serum lipids and fasting plasma glucose after 12 months. In addition, four studies found that LFDs may prevent T2D and reduce hypertensive medication for up to three years. Very-low-calorie diet were associated with the most weight loss after 12 months (-13.40kg, 95% CI -18.43 to -8.37kg) in one small study with beneficial effects on asthma. There was no evidence that PSMFs were associated with greater long-term weight loss than LCDs or VLCDs, but they were associated with greater lowering of fasting plasma glucose andHbA1c than LCDs.

Hession et al, 2009 (positive quality) performed a systematic review and meta-analysis to assess the weight-loss effects of low-CHO diets compared with low-fat/low-calorie diets. Randomized controlled trials conducted in adults with a body mass index (BMI) ≥28kg/m^2 that lasted for more than six months were included in the review. In addition, low-CHO diets were defined as “fewer grams per day of carbohydrate” and low-fat/low-calorie diets were defined as “<30% energy from fat,or -600kcal deficit diet.” At six months, weight change was -4.02kg in favor of the low-CHO diets compared to the low-fat/low-calorie diets (P<0.0001) and by 12 months, this difference was still significant at -1.05kg (P<0.05). Compared to low-fat/low-calorie diets, there were significant improvements inhigh-density lipoprotein (HDL) cholesterol (0.04mmol per L at six months and 0.06mmol per L at 12 months, P<0.05), triacylglycerols (-0.017mmol per L at six months and -0.19mmol per L at 12 months, P<0.05) andsystolic blood pressure (SBP) (-1.35mmHg at six months and -2.19mmHg at 12 months, P<0.05) for subjects following low-CHO diets. However, the high-CHO diets results in significant increases inTC (0.19mmol per L, P<0.0001) at six months and in LDL-C (0.14mmol per L and 0.37mmol per L) at six and 12 months respectively (P<0.00001) compared to the low-fat/low-calorie diets. There were no differences between the diets with respect todiastolic blood pressure (DBP) and fasting plasma glucose. There was also a higher attrition rate in the low-calorie/low-fat diets than the low-cCHO diets.

Nordmann et al, 2006 (positive quality) performed a meta-analysis to compare the effects of low-CHO diets without energy restriction to energy-restricted low-fat diets on weight loss, BP and lipid values in trials with dietary interventions with durations of at least six months. The final sample included five international RCTs. After six months, individuals assigned to low-CHO diets had lost more weight than individuals randomized to low-fat diets (weighted mean difference, -3.3kg; 95% CI -5.3, -1.4kg). This difference was no longer obvious after 12 months (weighted mean difference, -1.0kg; 95% CI -3.5, 1.5kg). There were no differences in BP. Triglyceride (TG) and HDL-C values changed more favorably in individuals assigned to low-CHO diets (after six months, for TG, weighted mean difference, -22.1mg per dL [-0.25mmol per L]; 95% CI -38.1, -5.3mg per dL [-0.43 to -0.06mmol/L]; and for HDL-C, weighted mean difference, 4.6mg per dL [0.12mmol per L]; 95% CI 1.5-8.1mg per dL [0.04-0.21mmol per L]), but TC and LDL-C values changed more favorably in individuals assigned to low-fat diets (weighted mean difference in LDL-C after six months, 5.4mg per dL [0.14mmol per L]; 95% CI 1.2-10.1mg per dL [0.03-0.26mmol per L]).

Primary Articles (12)

Randomized Controlled Trials (8)

Dale et al, 2009 (positive quality) conducted an RCT in New Zealand to compare the effectiveness of two support programs and two diets with differing macronutrient composition for long-term weight maintenance. Women who had lost 5% or more of their body weight were assigned to an intensive support program implemented by nutrition and activity specialists or to a nurse-led program involving "weigh-ins" and encouragement combined with either a high-CHO diet (55% CHO, 15-20% protein, 25-30% fat) or high-monounsaturated fat (MUFA) diet (40% CHO, 25% protein, 35% fat, 21% MUFA) diets. The final sample included 174 women (mean age 45 years; mean BMI 32kg/m^2) who were followed for two years, with 42 subjects in the high-CHO, intensive group, 45 in the high-MUFA, intensive group, 47 in the high-CHO, nurse group, and 40 in the high-MUFA, nurse group. Attrition rate was 13%. Average weight loss (approximately 2kg), did not differ between those in the support programs (0.1kg,95% CI -1.8, 1.9, P=0.95) or diets (0.7kg, 95% CI -1.1, 2.4, P=0.46). Total cholesterol and LDL-C levels were significantly higher among those on the high-MUFA diet (0.17mmol per L, P=0.040 and 0.16mmol per L, P=0.039, respectively), than those on the high-CHO diet.

Due et al, 2008 (positive quality) conducted an RCT conducted in Denmark to compared the effects of three diets on maintenance of an initial weight loss of at least 8% and risk factors forCVD and diabetes. Subjects were randomly assigned for six months to either a high-MUFA diet (45% CHO, 15% protein, 40% fat, >20% MUFA, N=54), a low-fat diet (60% CHO, 15% protein, 25% fat, N=51) or a control diet (50% CHO, 15% protein, 35% fat, N=26). All foods were provided for free from a purpose-built supermarket and subjects received two counseling sessions with a dietitian. The final sample included 106 subjects (mean age 28.2±4.8 years; meanBMI 31.5±2.6kg/m^2), with 39 subjects in the MUFA group, 43 in the low-fat group and 24 in the control group. Attrition rate was 13%. All groups regained weight (MUFA: 2.5±0.7kg; low-fat: 2.2±0.7kg; control: 3.8±0.8kg), but the groups did not differ. Body fat regain was lower in the LF (0.6±0.6%) and MUFA (1.6±0.6%) groups than in the control group (2.6±0.5%) (P<0.05). In the MUFA group,fasting insulin decreased by 2.6±3.5pmol per L, the HOMA insulin resistance by 0.17±0.13, and the ratio of LDL-C to HDL-C by 0.33±0.13; in the LF group, these variables increased by 4.3±3.0pmol per L (P<0.08) and 0.17±0.10 (P<0.05) and decreased by 0.02±0.09 (P=0.005), respectively; and in the control group, increased by 14.0±4.3pmol per L (P<0.001), 0.57±0.17 (P<0.001) and 0.05±0.14 (P=0.036), respectively.

Frisch et al, 2009 (positive quality) conducted an RCT in Germany to investigate whether the macronutrient composition of an energy-restricted diet influences the efficacy of a telemedically guided weight loss program. Subjects were assigned to either a low-CHO diet (<40% CHO, >35% fat, 25% protein) or a low-fat diet (<30% fat, >55% CHO, 15% protein). The intervention was delivered for six months, when subjects received nutrition education and dietary counseling by phone. Anthropometric, body composition and biochemical parameters were measured at baseline, six and 12 months. The final sample included 165 subjects (mean age 47±10.5 years; mean BMI=33kg/m^2). Attrition rate was 17%. In both groups, energy intake decreased by 400kcal per day within the first six months and increased slightly during the second six months. After six months, weight loss was not significantly different between groups, with the low-CHO group losing 7.2±5.4kg and the low-fat group losing 6.2±4.8kg. Between six and 12 months, weight regain between the groups was borderline significant, with the low-CHO group regaining less weight (1.6kg; 5.8±6.1kg lost) than the low-fat group (1.9kg; 4.3±5.1kg lost). In addition, TG (-0.03±0.55mmol per L vs. -0.18±0.40mmol per L; P<0.001) and HDL-C (-0.09±0.19mmol per L vs. -0.02±0.20mmol per L; P<0.001) levels were significantly lower at six months, and waist circumference (WC) (-4.7±8.9cm vs. -6.9±6.1cm; P<0.05) and SBP (-1±15mmHg vs. -5±14mmHg; P<0.01) were significantly lower at 12 months in the low-CHO group compared to the low-fat group.

Lim et al, 2009 (neutral quality) conducted a RCT in Australia to compare the changes in weight and other cardiovascular risk factors associated with three isocaloric energy-restricted diets to no-intervention control after one year. Subjects were randomly allocated to either very-low-CHO (VLC; 60% fat, 4% CHO, 36% protein; N=30), very-low-fat (VLF; 10% fat, 70% CHO, 20% protein; N=30), high-unsaturated fat (HUF; 30% fat, 20% protein, 50% CHO; N=30) with intensive support for three months followed by minimal support for 12 months, while the control group received no intervention. The final included 104 subjects (age 47±10 years; BMI of 32±6kg/m^2), with 30 subjects in the VLC group, 30 subjects in the VLF group, 30 subjects in the HUF group and 23 subjects in the control group. Attrition rate at 15 months was 34%. Weight change at three months did not differ between diet groups, and was -8.0±2.8kg for VLC, -6.7±3.5kg for VLF and -6.3±2.9kg for HUF. Weight change at 15 months did not differ between diet groups, and was -3.0±0.2kg for VLC, -2.0±0.1kg for VLF and -3.7±0.1kg for HUF and was significantly different from controls (+0.8±5.0kg; P<0.050. When all groups were combined, weight loss at 15 months was significantly correlated to a higher protein intake (r=-0.38, P=0.0009), lower fat intake (r=0.31, P=0.037) and higher fiber intake (r=-0.30, P=0.038). There were no significant differences in weight change or cardiovascular risk factors between groups.

McAuley et al, 2005 (positive quality) conducted a RCT in New Zealand to compare the effects on weight loss of consuming either a high-fat Atkins diet, a high-protein Zone diet, or high-CHO, high-fiber diet in obese, insulin-resistant women. The weeks one to eight of the study were intended to be a weight loss phase, weeks eight-16 were a weight maintenance phase with similar supervision as the weight loss phase, and for weeks 16 to 24 subjects were asked to continue following the intervention, but had no contact with the research team. None of the diets were formally energy-restricted and ad libitum consumption was advised for all subjects. The high-fat diet groups consumed 11% CHO, 29% protein, and 57% fat from one to eight weeks and 26% CHO, 24% protein and 46% fat from weeks eight to 24. The high-protein group consumed 34% CHO, 28% protein and 35% fat from weeks one to 24. The high-CHO group consumed 49% CHO, 21% protein, and 24% fat from weeks one to 24. The final sample included 84 women (mean age 45 years, mean BMI>27kg/m^2), 31 on the high-fat diet, 30 on the high-protein diet and 32 on the high-CHO diet. Attrition rate was 12%. There were no differences in reported energy in all groups during the six-month trial. Between baseline and eight weeks, the high-fat group (96.0±10.8kg to 89.4±10.3kg), the high-protein group (93.2±14.5kg to 87.8±13.7kg), and the high-CHO group (98.0±15.1kg to 93.7±14.5kg) all lost weight, with the high-fat and high-protein groups losing more weight than the high-CHO group. Between eight weeks and 24 weeks, the high-fat group (89.4±10.3kg to 88.9±10.6kg), the high-protein group (87.8±13.7kg to 86.3±14.2kg) and the high-CHO group (93.7±14.5kg to 93.3±14.5kg) all maintained their initial weight loss. Triglycerides decreased with all three diets, but the reductions were significantly greater in the high-fat diet and high-protein diet groups than the high-CHO group diet group. Insulin levels decreased in all three groups, with no differences between the groups. LDL-cholesterol levels were significantly higher in the high-fat diet group than in the high-protein diet group despite similar weight changes (P=0.02).

Sacks et al, 2009 (positive quality) conducted a RCT in the US to examine the effects on body weight of energy-reduced diets with differing macronutrient composition. Subjects were randomly assigned to one of four energy-reduced (-750kcal per day) diet groups: Low-fat, average protein (20% fat, 15% protein, 65% CHO), low-fat, high protein (20% fat, 25% protein, 55% CHO), high-fat, average protein (40% fat, 15% protein, 45% CHO) or high-fat, high-protein (40% fat, 25% protein, 35% CHO). Subjects were offered group and individual counseling session for two years and daily web-based food records were used to assess compliance with the study protocol. Weight measurements were taken at baseline, six months and two years. The final sample included 645 subjects (397 women, 248 men; mean age 52 years; mean BMI 33kg/m^2). Attrition rate at two years was 20%. After six months, participants had lost an average of 6kg (approximately 7% of initial weight), but began to regain weight after 12 months, with no differences between the groups. At two years, weight loss remained similar in those assigned to the 15% protein and 25% protein diets (-3.0 and -3.6kg, respectively); in those assigned to the 20% and 40% fat diets (-3.3kg for both groups); and in those assigned to the 65% and 35% CHO diets (-2.9 and -3.4kg, respectively) (P>0.20 for all comparisons). All the diets reduced risk factors for CVD and diabetes at six months and two years. The low-fat diets and the highest CHO diet decreased LDL-C levels more than the high-fat diets and the lowest CHO diet (P=0.0001). The lowest CHO diet increased HDL-C level more than the highest CHO diet (P=0.02). All the diets reduced TG levels and BP similarly, and all of the diets, except the highest CHO diet, decreased fasting serum insulin levels (P=0.07).

Shai et al, 2008 (positive quality) conducted an RCT in Israel to compare the effectiveness and safety of three diets with varying macronutrient composition. Subjects were randomly assigned to either a low-fat diet (50% CHO, 30% fat, 20% protein), a Mediterranean diet (50% CHO, 32% fat, 18% protein) and a low-CHO diet (40% CHO, 22% protein, 38% fat). The first six months of the trial was the weight loss phase, followed by 18 months of weight maintenance. Adherence to the study diets was assessed using a food-frequency questionnaire (FFQ). Weight was assessed monthly, but only 24-month data is reported. The final sample included 272 subjects (86% males; mean age 52 years; mean BMI 31kg/m^2). Attrition at two years was 16%. All groups lost weight over the 24-month trial; the low-CHO group lost -5.5±7.0kg, the Mediterranean-diet group lost -4.6±6.0kg, and the low-fat group lost -3.3±4.1kg (P=0.03 for the comparison between the low-fat and low-CHO groups at 24 months). All groups had significant decreases in BP, but the differences between groups were not significant. HDL-cholesterol increased in all groups over 24 months, with the low-CHO group increasing levels significantly more than the low-fat group (P<0.01). Triglyceride levels decrease more in the low-CHO groups compared to the low-fat group (P=0.03) and LDL-C did not change in any of the groups. The relative reduction in the TC: HDL-C ratio was 20% in the low-CHO group and 12% in the low-fat group (P=0.01). Among subjects with diabetes, changes in fasting plasma glucose and insulin levels were more favorable among those assigned to the Mediterranean diet than those assigned to the low-fat diet (P<0.001).

Tay et al, 2008 (positive quality) conducted an RCT in Australia to compare the effects on weight and CVD risk factors of moderate energy-restricted diets with different macronutrient composition. Subjects were randomly assigned to either a very-low-CHO, high-fat diet (VLCHF: 4% CHO, 35% protein, 61% fat) and a high-CHO, low-fat diet (HCLF: 46% CHO, 24% protein, 30% fat). Participants were provided with some food to enhance compliance with the dietary interventions and three-day food records were kept every two weeks to assess dietary intake. After the first eight weeks, subjects assigned to the VLCHF diet were then given the option to increase CHO intake to <40g per day for the remaining 16 weeks, while subjects assigned to the HCLF diet were asked to restrict saturated fat intake to <10g per day for the study duration. The final sample included 88 subjects completed the trial (aged 18 to 65 years; mean BMI 34kg/m^2), with 45 subjects in the VLCHF group and 43 in the HCLF group. Attrition rate was 19%. Weight loss was similar in both groups, as VLCHF subjects lost -11.9±6.3kg and HCLF subjects lost -10.1±5.7kg. Also, blood pressure, C-reactive protein (CRP), fasting glucose and insulin decreased similarly in both diet groups. However, the VLCHF diet produced greater decreases in triacylglycerols (P=0.01) and increases in HDL-C (P=0.002), while the HCLF diet produced a greater decrease in LDL-C (P<0.001).

Prospective Cohort Studies (4)

Halton et al, 2006 (positive quality) conducted a prospective cohort study in the US to examine the association between the low-CHO diet score and risk of CHD in subjects from the Nurses' Health Study. Subjects completed a FFQ and a low-CHO diet score was calculated based on the percentage of energy from CHO, fat and protein with higher scores reflecting higher fat and protein intake and lower CHO intake. Follow-up occurred over 20 years, and CHD incidence was determined using follow-up questionnaires and review of medical and death records. The final sample included 82,802 women (30-55 years of age at baseline). After multivariate adjustment, the relative risk of CHD between the lowest and highest deciles of CHO intake was not significantly different. Therefore, a low-CHO diet was not associated with risk of CHD over a 20-year period.

Halton et al, 2008 (positive quality) conducted a prospective cohort study in the US to examine the association between the low-CHO diet score and risk of T2D in subjects from the Nurses' Health Study. Subjects completed a FFQ and a low-CHO diet score was calculated based on the percentage of energy from CHO, fat and protein with higher scores reflecting higher fat and protein intake, and lower CHO intake. Follow-up occurred over 20 years, and T2D incidence was determined using follow-up questionnaires and review of medical and death records. The final sample included 85,059 women (30-55 years of age at baseline). After multivariate adjustment, the relative risk of T2D between the lowest and highest deciles of CHO intake was not significantly different. Therefore, a low-CHO diet was not associated with risk of T2D over a 20-year period.

Lagiou et al, 2007 (neutral quality) conducted a cohort study in Sweden to examine whether low-CHO, high-protein diets are associated with increased mortality in

subjects from the Women's Lifestyle and Health Cohort Study. Subjects completed a FFQ at baseline; food and beverage items were used to calculate CHO and protein scores (one (low intake) to 10 (high intake)) based on deciles of intake. Mortality was determined using the Swedish nationwide health registers and the Swedish Case of Death Register. The final sample included 42,237 women (aged 30-49 years at baseline) who were followed-up for an average of 12 years. Percentage of energy intake from CHO ranged from 72% (10th percentile) to 23% (90th percentile). Percentage of energy intake from protein ranged from 10.4% (10th percentile) to 23.0% (90th percentile). Decreasing CHO or increasing protein by one decile were associated with increased total mortality by 6% (95% CI 0% to 12%) and 2% (95% CI 1% to 5%), respectively. Decreasing CHO or increasing protein by one decile were also associated with increased cardiovascular mortality by 13% (95% CI -4 to 32%) and 16% (95% CI 5% to 29%), respectively.

Trichopoulou et al, 2007 (positive quality) analyzed data from Greek participants (N=22,944) in a prospective cohort study [European Prospective Investigation in Cancer and Nutrition (EPIC)] to examine the mortality of individuals according to their CHO and protein intake. Dietary data was collected using a validated, interviewer-administered, 150-item FFQ focused on the year prior to enrollment. Mortality was determined using date and cause of death from death certificates and other official sources. A LC/HP (low-CHO, high-protein) score was calculated for each subject, with a higher score implying higher protein and lower CHO intake. Results showed that an increasing LC/HP score was significantly associated with mortality (RR 1.08; 95% CI 1.03, 1.13; P=0.001) (adjusted for sex, age, years of schooling, smoking, BMI, physical activity, ethanol intake and total energy intake). Individuals with habitual diets low in CHOs and high in protein tend to have higher overall mortality compared to individuals with habitual diets high in CHOs and low in protein. This increase in mortality was not concentrated to particular causes, but was significant only with respect to cardiovascular deaths.

View table in new window

Author, Year, Study Design, Class, Rating	Population	Intervention (Initial / Intense Phase)	Intervention (Follow Up / Maintenance Phase)	Macronutrient Composition of Diet	Weight Outcomes (End of Initial / Intense Phase)	Weight Outcomes (End of F/U / Maintenance Phase)	Safety Outcomes
Avenell A et al 2004 Study Design: Systematic Review Class: M Rating:	N=26 RCTs.	All studies included in the review were carried out for more than one year.	Not applicable.	Low-fat diets: Advice given to reduce fat, >6.7mJ per day. Low-calorie diets (LCD): 4.2-6.7mJ per day. Very-low-calorie diets (VLCD): <4.2mJ per day. Protein-sparing modified fast (PSFM): ≤40g per day of CHO.	LFDs produced significant weight losses up to 36 months (-3.55kg, 95% CI -4.54 to -2.55kg). VLCDs were associated with the most weight loss after 12 months (-13.40kg, 95% CI -18.43 to -8.37kg) in one small study. There was no evidence that PSMFs were associated with greater long-term weight loss than LCDs or VLCDs.	Not applicable.	LFDs improved BP, serum lipids, and fasting plasma glucose after 12 months and four studies found that LFDs may prevent T2D and ↓ hypertensive medication for up to three years. VLCDs were associated with beneficial effects on asthma. PSMFs were associated with greater lowering of fasting plasma glucose and HbA1c than LCDs.
Dale KS et al 2009 Study Design: Randomized Controlled Trial Class: A Rating:	N=174 women. • N=42 in the high-CHO, intensive group • N=45 in the high-MUFA, intensive group • N=47 in the high-CHO, nurse group • N=40 in the high-MUFA, nurse group. Age: 45 years. BMI: 32kg/m^2 Attrition rate: 13%.	Not applicable.	Women who had lost more than 5% weight were assigned to an support program implemented by nutrition and activity specialists or to a nurse-led program involving "weigh-ins" and encouragement combined with either a high-CHO diet or high-MUFA diet diets. Women were followed for two years.	Intensive and high-CHO: 55% CHO, 25-30% protein, 15-20% fat. Intensive and high-fat: 55% CHO, 25-30% protein, 15-20% fat. Nurse and high-CHO: 40% CHO, 35% protein, 25% fat. Nurse and high-fat: 40% CHO, 35% protein, 25% fat.	Not applicable.	Average weight loss (approximately 2kg) did not differ between those in the support programs (0.1kg, 95% CI -1.8, 1.9, P=0.95) or diets (0.7kg, 95% CI -1.1, 2.4, P=0.46).	TC and LDL-C levels were significantly higher among those on the high-MUFA diet (0.17mmol/L, P=0.040 and 0.16mmol/L, P=0.039, respectively), than those on the high-CHO diet.
Due A et al 2008 Study Design: Randomized Controlled Trial	N=106 subjects. Mean age: 28 years. Mean BMI: 32kg/m^2. N=39 subjects in the MUFA	Not applicable.	Subjects who had lost more than 8% body weight were randomly assigned for six months to either a high-MUFA	High-MUFA: 45% CHO, 40% protein, 15% fat. Low-fat: 60%CHO, 25% protein, 15% fat.	Not applicable.	All groups regained weight (MUFA: 2.5±0.7kg; low-fat: 2.2±0.7kg; control: 3.8±0.8kg), but the groups did not differ. Body fat regain was	In the MUFA group, fasting insulin ↓ by 2.6±3.5pmol/L, the HOMA insulin resistance by 0.17±0.13, and the ratio of LDL to HDL by 0.33±0.13.

Class: A Rating:	group; N=43 in the low-fat group; and N=24 in the control group. Attrition rate: 13%.		diet, a low-fat diet or a control diet. All foods were provided for free from a purpose-built supermarket and subjects received two counseling sessions with a dietitian.	Control: 50% CHO, 35% protein, 15% fat.		lower in the LF (0.6±0.6%) and MUFA (1.6±0.6%) groups, than in the control group (2.6±0.5%) (P<0.05).	In the LF group, these variables ↑ by 4.3±3.0pmol/L (P<0.08) and 0.17±0.10 (P<0.05) and ↓ by 0.02±0.09 (P=0.005), respectively. In the control group, ↑ by 14.0±4.3pmol/L (P<0.001), 0.57±0.17 (P<0.001) and 0.05±0.14 (P=0.036), respectively.
Frisch S et al 2009 Study Design: Randomized Controlled Trial Class: A Rating:	N=165. Age: 47 years. BMI: 33kg/m^2. Attrition rate: 17%.	Subjects were assigned to a calorie-restricted diet (approximately -400kcal per day) that was either low-CHO or low-fat. The intervention was delivered for six months, when subjects received nutrition education and dietary counseling by phone. Anthropometric, body composition and biochemical parameters were measured at baseline and six months.	The weekly telephone counseling was discontinued during months six to 12. Anthropometric, body composition and biochemical parameters were measured at 12 months.	Low-CHO: <40% CHO, >35% protein, 25% fat. Low-fat: >55% CHO, <30% protein, 15% fat.	After six months, weight loss was NS different between groups. The low-CHO group lost 7.2±5.4kg, and the low-fat group lost 6.2±4.8kg.	Between six and 12 months, weight regain between the groups was borderline significant (P<0.05), with the low-CHO group regaining less weight (1.6kg; 5.8±6.1kg lost) than the low-fat group (1.9kg; 4.3±5.1kg lost).	TG (-0.03±0.55mmol/l vs. -0.18±0.40mmol/l; P<0.001) and HDL-C (-0.09±0.19mmol/L vs. -0.02±0.20mmol/L; P<0.001) were significantly lower at six months. WC (-4.7±8.9cm vs. -6.9±6.1cm; P<0.05) and SBP (-1±15mmHg vs. -5±14mmHg; P<0.01) were significantly lower at 12 months in the low-CHO group compared to the low-fat group.
Halton et al 2006 Study Design: Prospective Cohort Study Class: B Rating:	N=82,802 women. Age: 30-55 years at baseline. Nurses' Healthy Study.	Subjects completed a FFQ and a low-CHO diet score was calculated based on the percentage of energy from CHO, fat, and protein, with higher scores reflecting higher fat and protein intake, and lower CHO intake. Follow-up occurred over 20 years, and CHD incidence was determined using follow-up questionnaires, and review of medical and death records.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	After multivariate adjustment, the RR of CHD between the lowest and highest deciles of CHO intake was NS different.

Halton TL, Liu S et al, 2008 Study Design: Prospective cohort Class: B Rating:	N=85,059 women. Age: 30-55 years at baseline. Nurses' Health Study.	Subjects completed a FFQ and a low-CHO diet score was calculated based on the percentage of energy from CHO, fat, and protein, with higher scores reflecting higher fat and protein intake, and lower CHO intake. Follow-up occurred over 20 years, and CHD incidence was determined using follow-up questionnaires, and review of medical and death records.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	After multivariate adjustment, the relative risk of T2D between the lowest and highest deciles of CHO intake was NS different.
Hession M et al 2009 Study Design: Systematic Review Class: M Rating:	N=50 RCTs conducted in adults with BMI $\geq 28 kg/m^2$ lasting for more than six months.	Not applicable.	Not applicable.	Low-CHO: <60g per day CHO. Low-fat, low-calorie: <30% fat.	At six months, weight Δ was -4.02kg in favor of the low-CHO diets, compared to the low-fat/low-calorie diets (P<0.0001).	At 12 months, weight loss was still significantly less in the low-CHO diets, compared to the low-fat diets at -1.05kg (P<0.05)	Compared to low-fat/low-calorie diets, there were significant improvements in HDL-C (0.04mmol/L at six months and 0.06mmol/L at 12 months, P<0.05), triacylglycerols (0.017mmol/L at six months and -0.19mmol/L at 12 months, P<0.05) and SBP (-1.35mmHg at six months and -2.19mmHg at 12 months, P<0.05) for subjects following low-CHO diets. The high-CHO diets resulted in significant ↑ in to TC (0.19mmol/L, P<0.0001) at six months, and in LDL-C (0.14mmol/L and 0.37mmol/L) at six and 12 months, respectively (P<0.00001), compared to the low-fat/low-calorie diets.
Lagiou et al 2007 Study Design: Cohort Study Class: B Rating:	N=42,237 women from the Women's Lifestyle and Health Cohort Study. Age: 30-49 years at baseline. Followed for an average of 12 years.	Subjects completed a FFQ at baseline; food and beverage items were used to calculate CHO and protein scores [one (low intake) to 10 (high intake)] based on deciles of intake. Mortality was determined using	Not applicable.	Percentage of energy intake from CHO ranged from 72% (10th percentile) to 23% (90th percentile). Percentage of energy intake from protein ranged from 10.4% (10th percentile) to	Not applicable.	Not applicable.	Decreasing CHO or increasing protein by one decile were associated with ↑ total mortality by 6% (95% CI 0% to 12%) and 2% (95% CI -1% to 5%), respectively. Decreasing CHO or increasing protein by one decile were associated with ↑ cardiovascular mortality by 13%

		the Swedish nationwide health registers and the Swedish Case of Death Register.		23.0% (90th percentile).			(95% CI -4% to 32%) and 16% (95% CI 5% to 29%), respectively.
Lim et al 2009 Study Design: Randomized Controlled Trial Class: A Rating:	N=104 subjects. Age: 47 years. BMI: 32kg/m^2. N=30 subjects in the VLC group, N=30 subjects in the VLF group, N=30 subjects in the HUF group and N=23 subjects in the control group. Attrition rate at 15 months: 34%.	Subjects were randomly allocated to either very-low-CHO (VLC), very-low-fat (VLF), high-unsaturated fat (HUF) with intensive support for three months, while the control group received no intervention.	The intensive three months initial phase was followed by minimal support for 12 months.	VLC: 4% CHO, 60% protein, 35% fat. VLF: 70% CHO, 10% protein, 20% fat. HUF: 50% CHO, 30% protein, 20% fat.	Weight Δ at three months did not differ between diet groups and was -8.0±2.8kg for VLC, -6.7±3.5kg for VLF, and -6.3±2.9kg for HUF.	Weight Δ at 15 months did not differ between diet groups, and was -3.0±0.2kg for VLC, -2.0±0.1kg for VLF, and -3.7±0.1kg for HUF and was significantly different from controls (+0.8±5.0kg; P<0.050). For all groups combined, weight loss at 15 months was significantly correlated to a higher protein intake (r=-0.38, P=0.0009), lower fat intake (r=0.31, P=0.037) and higher fiber intake (r=-0.30, P=0.038).	At 15 months, there were NS differences in weight Δ or cardiovascular risk factors between groups.
McAuley KA et al 2005 Study Design: Randomized Controlled Trial Class: A Rating:	N=84 obese, insulin-resistant women. Age: 45 years. BMI:>27kg/m^2. N=31 on the high-fat diet; N=30 on the high-protein diet; N=32 on the high-CHO diet. Attrition rate: 12%.	Weeks one to eight of the study were a supervised weight loss phase. Subjects were randomized to one of three diet intervention, either a high-fat diet (Atkins), a high-protein diet (Zone) or a high-CHO, high-fiber diet; none of the diets were formally energy-restricted and ad libitum consumption was advised for all subjects.	Weeks eight-16 were a supervised weight maintenance phase. Weeks 16-24 were an unsupervised weight maintenance phase.	High-fat: 11% CHO, 57% protein, 29% fat. High-protein: 34% CHO, 35% protein, 28% fat. High-CHO: 49% CHO, 24% protein, 21% fat.	Between baseline and eight weeks, the high-fat group (96.0±10.8kg to 89.4±10.3kg), the high-protein group (93.2±14.5kg to 87.8±13.7kg) and the high-CHO group (98.0±15.1kg to 93.7±14.5kg) all lost weight, with the high-fat and high-protein groups losing more weight than the high-CHO group.	Between eight weeks and 24 weeks, the high-fat group (89.4±10.3kg to 88.9±10.6kg), the high-protein group (87.8±13.7kg to 86.3±14.2kg), and the high-CHO group (93.7±14.5kg to 93.3±14.5 kg) all maintained their initial weight loss.	TG ↓ with all three diets, but the reductions were significantly greater in the high-fat diet and high-protein diet groups than the high-CHO group diet group. Insulin levels ↓ in all three groups, with no differences between the groups. LDL-C levels were significantly higher in the high-fat diet group than in the high-protein diet group, despite similar weight Δs (P=0.02).
Nordmann AJ et al 2006 Study Design: Meta-analysis Class: M Rating:	N=5 RCTs, with a total of 447 subjects.	A meta-analysis was done to compare the effects of low-CHO diets without energy restriction to energy-restricted low-fat diets on weight loss, BP, and lipid values in trials with dietary interventions with durations of at least six months.	Not applicable.	Low-CHO: <60g per day CHO. Low-fat: <30% fat.	After six months, individuals assigned to low-CHO diets had lost more weight than individuals randomized to low-fat diets (weighted mean difference, -3.3kg; 95% CI -5.3, -1.4kg).	The difference in weight loss between diets at six months was no longer obvious after 12 months (weighted mean difference, -1.0kg; 95% CI -3.5, 1.5kg).	There were no differences in BP. TG and HDL-C values changed more favorably with low-CHO diets (after six months, for TG, weighted mean difference, -22.1mg/dL [-0.25mmol/L]; 95% CI -38.1, -5.3mg/dL [-0.43 to -0.06mmol/L]; for HDL-C, weighted mean difference, 4.6mg/dL [0.12mmol/L]; 95% CI

							1.3-8.1mg/dL [0.04-0.21mmol/L]). But TC and LDL-C values changed more favorably with low-fat diets (weighted mean difference in LDL-C after six months, 5.4mg/dL [0.14mmol/L]; 95% CI 1.2-10.1mg/dL [0.03-0.26mmol/L]).
Sacks FM, Bray GA et al, 2009 Study Design: Randomized clinical trial Class: A Rating:	N=645 subjects (397 women, 248 men). Age: 52 years. BMI: 33kg/m^2. Attrition rate at two years: 20%.	Subjects were randomly assigned to one of four energy-reduced (-750kcal per day) diet groups: Low-fat, average protein, low-fat, high protein, high-fat, average protein or high-fat, high-protein. Subjects were offered group and individual counseling session for two years and daily web-based food records were used to assess compliance with the study protocol. Weight measurements were taken at baseline, six months and two years.	Not applicable.	Low-fat, average protein: 65% CHO, 20% protein, 15% fat. Low-fat, high-protein: 55% CHO, 20% protein, 25% fat. High-fat, average protein: 45% CHO, 40% protein, 15% fat. High-fat, high-protein: 35% CHO, 40% protein, 25% fat.	At six months all groups lost a similar amount of weight (6kg or approximately 7% of initial weight), but began to regain weight after 12 months.	At two years, weight loss remained similar in those assigned to the 15% protein and 25% protein diets (-3.0 and -3.6kg, respectively); in those assigned to the 20% and 40% fat diets (-3.3kg for both groups); and in those assigned to the 65% and 35% CHO diets (-2.9 and -3.4kg, respectively) (P>0.20 for all comparisons).	All diets reduced CVD and diabetes risk factors at six months and two years. The low-fat diets and the highest CHO diet ↓ LDL-C levels more than the high-fat diets and the lowest CHO diet (P=0.0001). The lowest CHO diet ↑ HDL level more than the highest CHO diet (P=0.02). All the diets ↓ TG levels and BP similarly, and all diets, except the highest CHO diet, ↓ fasting serum insulin levels (P=0.07).
Shai et al 2008 Study Design: Radomized Controlled Trial Class: A Rating:	N=272 subjects (86% males). Age: 52 years. BMI: 31kg/m^2. Attrition at two years: 16%.	Subjects were randomly assigned to either a low-fat diet, a Mediterranean diet and a low-CHO diet. The first six months of the trial was the weight loss phase, followed by 18 months of weight maintenance. Adherence to the study diets was assessed using a FFQ. Weight was assessed monthly, but only 24 month data is reported.	Not applicable.	Low-CHO: 40% CHO, 38% protein, 22% fat. Mediterranean Diet: 50% CHO, 32% protein, 18% fat. Low-CHO: 40% CHO, 38% protein, 22% fat.	Not reported in this paper.	All groups lost weight over the 24-month trial. The low-CHO group lost -5.5±7.0kg, the Mediterranean-diet group lost -4.6±6.0kg and the low-fat group lost -3.3±4.1kg (P=0.03 for the comparison between the low-fat and low-CHO groups at 24 months)	All groups ↓ BP, but between group differences were NS. HDL-C ↑ in all groups, with the low-CHO group increasing levels more than the low-fat group (P<0.01). TG levels ↓ more in the low-CHO groups compared to the low-fat group (P=0.03) and LDL-C did not Δ in any of the groups. TC:HDL ratio ↓ 20% in the low-CHO group and 12% in the low-fat group (P=0.01). In subjects with diabetes, Δs in fasting plasma glucose and insulin levels were more favorable among those assigned to the Mediterranean diet than those assigned to

							the low-fat diet (P<0.001).
Tay et al 2008 Study Design: Randomized Clinical Trial Class: A Rating:	N=88 subjects completed the trial. Age: 18 to 65 years. BMI: 34kg/m^2. N=45 subjects in the VLCHF group; N=43 in the HCLF group. Attrition rate: 19%.	Subjects were randomly assigned to either a very-low-CHO, high-fat diet (VLCHF) and a high-CHO, low-fat diet (HCLF). Participants were provided with some food to enhance compliance with the dietary interventions and three-day food records were kept every two weeks to assess dietary intake.	Not applicable.	VLCHF: 4% CHO, 61% protein, 35% fat. HCLF: 46% CHO, 30% protein, 24% fat.	Weight loss was similar in both groups, as VLCHF subjects lost -11.9±6.3kg and HCLF subjects lost -10.1±5.7kg.	Not applicable.	BP, CRP, fasting glucose and insulin ↓ similarly in both diet groups. The VLCHF diet produced greater ↓ in triacylglycerols (P=0.01) and ↑ in HDL-C (P=0.002), while the HCLF diet produced a greater ↓ in LDL-C (P<0.001).
Trichopoulou A, Psaltopoulou T et al, 2007 Study Design: Prospective Cohort Study Class: B Rating:	N=22,944 Women and men aged 20-86 years at the time of enrollment between 1993-1999.	Prospective cohort study in which follow-up was performed from 1993 to 2003 to evaluate the effects of diet on mortality. Participants were distributed by increasing deciles according to protein intake or CHO intake, as well as by an additive score (low CHO/high protein=LC/HP score) generated by increasing decile intake of protein and decreasing decile intake of CHOs.	Not applicable.	A LC/HP score was calculated for each subjectsm based on CHO and protein intake estimated using a 150-item FFQ. A high score implies higher protein, lower CHO intake.	Not applicable.	Not applicable.	An increasing LC/HP score was significantly associated with mortality (1.08 (1.03, 1.13); P=0.001) (adjusted for sex, age, years of schooling, smoking, BMI, physical activity, ethanol intake and total energy intake). This ↑ in mortality was not concentrated to particular causes, but was significant only with respect to cardiovascular deaths.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets

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